REMARKS

This Amendment is responsive to the Office Action mailed September 4, 2007. By this Amendment, Applicants amend claims 1, 8-13, 16, 24, 34, 35, 38, 42, 43, 48, 51, and 53; and cancel claims 2-7, 14, 15, 17-23, 25-33, 36, 37, 39-41, 44-47, 49, 50, 52, and 54-56. Claims 1, 8-13, 16, 24, 34, 35, 38, 42, 43, 48, 51, and 53 are pending. Claims 1, 8-13, 16, 24, 34, 35, 42, 43, 48, 51, and 53 are under consideration. Claim 38 is withdrawn.

Reconsideration and withdrawal of the rejections made in the above-referenced Office Action are respectfully requested in view of the following amendments and remarks. Support for the amendments as filed can be found in the specification and claims as filed, e.g., original claims 1, 19, 28, and 51-53; page 49, lines 3-24; and page 50, Table 3.

Election/Restriction

Applicants thank the Examiner for reconsideration of the requirement for election/restriction set forth in the paper mailed September 4, 2007. Applicants note that the restriction requirement is made final, but are allowing non-elected subject matter to remain pending, subject to rejoinder at the Examiner's discretion.

Information Disclosure Statement

Applicants also thank the Examiner for acknowledgement of receipt of the Information Disclosure Statements filed December 15, 2006; April 10, 2007; and May 10, 2007. In addition, Applicants thank the Examiner for consideration of all the documents listed in the Information Disclosure Statements filed December 15, 2006 and May 10, 2007.

With regard to the Information Disclosure Statement filed April 10, 2007, the Office Action asserts that documents 20 and 21 were not considered because the documents have not been provided.

Applicants respectfully submit that full length documents corresponding to the chemical abstracts listed on the Form PTO-1449 were indeed filed with the IDS on April 10, 2007. However, for the Examiner's convenience, Applicants submit herewith copies of the previously unconsidered documents.

Claim Objections

The Examiner objects to claims 1, 2, 4, 5, 8-19, 23-28, 34-37, and 39-46 as allegedly containing non-elected subject matter. Applicants note that the claims have been amended and that further examination has been greatly simplified. Applicants therefore respectfully request that the Examiner rejoin the non-elected subject matter remaining in the pending claims.

Claim Rejections – 35 U.S.C. § 112, First Paragraph

The Office Action rejects claims 1, 2, 4, 5, 8-19, 23-28, 34-37, and 39-46 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description and enablement requirements. In particular, the Office Action asserts that the claims have written description support and are enabled for compounds of Formula I wherein:

Z is sulfur;

R^1 is substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, or $-C(=W)R^5$ where W is oxygen, and R^5 is a hydrogen atom, alkyl, furan, pyrazine, thiophene, pyrrole, indole, or phenyl;

R^2 is a hydrogen atom, substituted or unsubstituted lower alkyl, or $-C(=W^1)R^{12}$ wherein W^1 is oxygen and R^{12} is a hydrogen atom, or a substituted or unsubstituted lower alkyl;

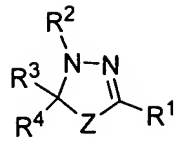
R^3 is a hydrogen atom, unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, phenyl, or piperazine; and

R^4 is phenyl.

In response, with regard to the enablement requirement, Applicants submit the instant disclosure describes compounds which demonstrate inhibition of human colon carcinoma cells (see, e.g., Test Example 1 at pages 49, and Table 3 at page 52). The instant specification also sets forth examples of compounds which inhibit Eg5 activity (see, e.g., Test Example 3, pages 51-53, particularly page 52, first full paragraph). The disclosure also provides that human Eg5 is expressed more intensely in tumor tissue than in normal tissue (see specification at page 2, last full paragraph), and that compounds capable of human Eg5 inhibition were known at the time of Applicants filing (see, e.g., specification at page 3, 2nd paragraph).

Moreover, the state of the art at the time of Applicants' filing recognized the therapeutic potential of Eg5 inhibitors (see, e.g., specification at page 3, first paragraph). This is in contrast to the Office's reliance on Pinkerton et al (*Bioorganic and Medicinal Chemistry Letters* **17**:3562-3569, 2007) which describes studies performed with compounds distinct from those claimed. Furthermore, the Pinkerton document does not address whether or not the claimed compounds are enable for methods for therapeutic treatment of colon cancer.

Applicants further submit that the breadth of the claims is supported by the instant disclosure. Claim 1 recites a method for therapeutic treatment of a colon cancer which comprises administering an effective amount of a compound represented by the general formula (I), or a pharmacologically acceptable salt thereof as an active ingredient:



(I)

<wherein

Z represents a sulfur atom;

R^1 represents substituted or unsubstituted phenyl;

R^2 represents a

hydrogen atom,

substituted or unsubstituted lower alkyl, or

$-C(=W^1)R^{12}$ [wherein W^1 represents an oxygen atom or a sulfur atom, R^{12} represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, a substituted or unsubstituted heterocyclic group, $-Y^1R^{13}$ (wherein Y^1 represents an oxygen atom or a sulfur atom, and R^{13} represents substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group), or $-NR^{14}R^{15}$ (wherein R^{14} and R^{15} are the same or different, and represent a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group, or R^{14} and R^{15} are combined together with the adjacent nitrogen atom to form a substituted or unsubstituted heterocyclic group)];

R^3 represents substituted or unsubstituted lower alkyl; and

R^4 represents substituted or unsubstituted phenyl>. Thus, the claimed compounds are in accord with the scope indicated in the Office Action with regard to R^1, R^3 and R^4. Furthermore, the claimed compounds, including the full scope of the claimed substituents of R^2, are clearly enabled for at least their claimed use in methods for therapeutic treatment for colon cancer insofar as the specification describes such compounds and methods of making the same.

In response to the Office's assertion at page 11 of the Action that no working examples or direction have been provided, Applicants submit that *both* working examples *and* direction have been set forth in the instant specification. The Office need look no further than Applicants' elected species, Compound 49, disclosed, e.g., at Example 36 on page 67 for such an example. Furthermore, at page 6, Section II of the Action, the Office sets forth a long list of examples which have been reduced to practice. This list includes compounds as claimed with myriad substituents at R^1, R^2, and R^3. Thus, the assertion that no direction and/or working examples have been provided is contradicted by the Office's own assessment of the instant invention.

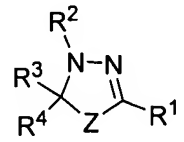
Based on at least the foregoing, Applicants submit that the claims are in compliance with the enablement requirement and respectfully request withdrawal of the rejection under 35 U.S.C. § 112, first paragraph.

With regard to the written description requirement, Applicants submit that the specification fully describes the claimed compounds and methods for at least the reasons set forth above. In particular, Applicants submit that the specification discloses examples of compounds wherein R^1 is a substituted phenyl at Table 1, pages 45-46 (see, e.g., compounds 49, 55, 61, and 62). Moreover, the specification discloses methods of preparing compounds wherein

each of R^1 and R^4 are a substituted or ubsubstituted phenyl (see, e.g., page 67, Example 36). Furthermore, the disclosure presents examples of compounds which have anti-tumor activity and/or Eg5 inhibitory activity (see specification at, e.g., page 50, Table 3; and first full paragraph of page 52). Based upon such disclosure, one of ordinary skill in the art would know which compounds having a substituted or unsubstituted phenyl at R^1 and R^4 with the claimed structure would be expected to have anti-tumor activity and/or Eg5 inhibitory activity.

Furthermore, because the specification discloses methods of making the claimed products wherein R^1 and R^4 are substituted or unsubstituted phenyl, and R^3 is a substituted or unsubstituted lower alkyl, one of ordinary skill in the art would recognize that Applicants were in possession of such compounds with R^2 substituents as claimed.

As mention above, claim 1 recites a method for therapeutic treatment of a colon cancer which comprises administering an effective amount of a compound represented by the general formula (I), or a pharmacologically acceptable salt thereof as an active ingredient:



(I)

<wherein

Z represents a sulfur atom;

R^1 represents substituted or unsubstituted phenyl;

R^2 represents a

hydrogen atom,

substituted or unsubstituted lower alkyl, or

$-C(=W^1)R^{12}$ [wherein W^1 represents an oxygen atom or a sulfur atom, R^{12} represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, a substituted or unsubstituted heterocyclic group, $-Y^1R^{13}$ (wherein Y^1 represents an oxygen atom or a sulfur atom, and R^{13} represents substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group), or $-NR^{14}R^{15}$ (wherein R^{14} and R^{15} are the same or different, and represent a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group, or R^{14} and R^{15} are combined together with the adjacent nitrogen atom to form a substituted or unsubstituted heterocyclic group)];

R^3 represents substituted or unsubstituted lower alkyl; and

R^4 represents substituted or unsubstituted phenyl>. Applicants submit that the compounds disclosed in the instant specification are representative of the genus of compounds claimed. Furthermore the compounds of the presently claimed invention, wherein R^1 is a substituted or unsubstituted phenyl, R^3 represents substituted or unsubstituted lower alkyl, and R^4 represents substituted or unsubstituted phenyl, are in line with the Examiner's comments, Moreover, the claimed substituents for R^2 are also fully described in the instant specification.

Based at least on the foregoing, Applicants submit that the claimed invention has full written description support, and respectfully request withdrawal of both the enablement and written description rejections under 35 U.S.C. § 112, first paragraph.

Claim Rejections – 35 U.S.C. § 112, Second Paragraph

The Office Action rejects claims 1, 23-28, 34-37, and 39-56 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In response, Applicants have amended the claims to render them even clearer and more definite. However, Applicants' amendment does not express any agreement or acquiescence with the rejection of record.

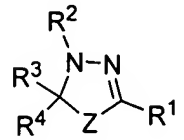
Claim Rejections – 35 U.S.C. § 101 and 35 U.S.C. § 112

The Office Action rejects claims 49, 50, and 54-56 under 35 U.S.C. § 112, as allegedly indefinite and under 35 U.S.C. § 101 as allegedly directed to non-statutory subject matter. Applicants respectfully submit that the amendment addresses the instant rejection and respectfully request withdrawal of the rejection.

Claim Rejections – 35 U.S.C. § 102(b)

The Office Action rejects claims 1, 2, 4, 5, 8, 17-19, 23-28, and 39-46 under 35 U.S.C. § 102(b) as allegedly anticipated by Holmberg (RN 859460-84-7; hereinafter "HOLMBERG"). Applicants submit that the claims define novel subject matter. Claim 1 recites recites a method for therapeutic treatment of a colon cancer which comprises administering an effective amount

of a compound represented by the general formula (I), or a pharmacologically acceptable salt thereof as an active ingredient:



(I)

<wherein

Z represents a sulfur atom;

R^1 represents substituted or unsubstituted phenyl;

R^2 represents a

hydrogen atom,

substituted or unsubstituted lower alkyl, or

$-C(=W^1)R^{12}$ [wherein W^1 represents an oxygen atom or a sulfur atom, R^{12} represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, a substituted or unsubstituted heterocyclic group, $-Y^1R^{13}$ (wherein Y^1 represents an oxygen atom or a sulfur atom, and R^{13} represents substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group), or $-NR^{14}R^{15}$ (wherein R^{14} and R^{15} are the same or different, and represent a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic

group, or R^{14} and R^{15} are combined together with the adjacent nitrogen atom to form a substituted or unsubstituted heterocyclic group)];

R^3 represents substituted or unsubstituted lower alkyl; and R^4 represents substituted or unsubstituted phenyl>. HOLMBERG discloses a compound in which R^3 is hydrogen. For at least this reason, HOLMBERG does not anticipate the instant claims, and Applicants respectfully request withdrawal of the rejection.

Conclusion

In view of the foregoing, the Examiner is respectfully requested to reconsider and withdraw the rejections of record, and allow all the pending claims.

No additional fee is believed due at this time. If, however, any additional fee is necessary to ensure consideration of the submitted materials, the Patent and Trademark Office is hereby authorized to charge the same to Deposit Account No. 19-0089.

Should there be any questions, the Examiner is invited to contact the undersigned at the below listed telephone number.

Respectfully submitted,
Chikara MURAKATA et al.

Bruce H. Bernstein
Reg. No. 29,027

Stephen M. Roylance
Reg. No. 31,296

February 28, 2008
GREENBLUM & BERNSTEIN, P.L.C.
1950 Roland Clarke Place
Reston, VA 20191
(703) 716-1191